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REMARKS/ARGUMENTS

The Applicants first acknowledge with appreciation the telephone interview granted to the undersigned by Examiners Upreti and Wu on December 15, 2005, and the follow-up discussion with Examiner Upreti on December 16, 2005. In light of the interviews, the amendments to the claims presented herein and the following remarks, reexamination and reconsideration of this application, withdrawal of the rejections, and formal notification of the allowability of all claims as presented are earnestly solicited. As detailed in the Office Action mailed October 21, 2005, Claims 1-90 are pending, wherein Claims 1-90 have been rejected. In response to the Office Action, Claims 1, 3, 14, 16, 26, 41, 55, 57, 64, and 77 have been amended and Claims 2, 15, and 56 have been cancelled (incorporated into Claims 1, 14, and 55, respectively). The amendments to the claims find support throughout the Specification and the Drawings and no new matter has been added. Accordingly, it is believed that the claims now define patentable subject matter over the prior art cited in the Office Action and notice to such effect is requested at the Examiner's earliest convenience.

Claim Rejections – 35 U.S.C. §103

Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 were rejected in the Office Action as being obvious over background disclosure in the present application ("the primary reference") in view of U.S. Patent No. 4,997,769 to Lundsgaard and further in view of U.S. Patent No. 5,835,617 to Ohta *et al.* The Applicants respectfully traverse these rejections. However, the Applicants have amended Claims 1, 3, 14, 16, 26, 41, 55, 57, 64, and 77 to further clarify the subject matter being claimed. In conjunction with these amendments, Claims 2, 15, and 56 have been incorporated into Claims 1, 14, and 55, respectively, and, as such, Claims 2, 15, and 56 have been cancelled. These amendments find support throughout the Specification and the Drawings and no new matter has been added.

The background of the present application notes that a particular molecule may undergo a reaction with a particular dye to experience a change in color. In addition, it is sometimes desirable to be able to determine an amount of a particular molecule in a sample. Further, a color

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CCD digital camera can be used in combination with a microscopy system to capture images of a sample in the Red, Green and Blue channels (RGB) of the color CCD camera.

The Lundsgaard '769 patent discloses a method and apparatus for determining oxygen saturation or oxygen content of a blood sample by determining a total of five hemoglobin derivatives. The apparatus 10 includes a conduit system comprising an inlet tube 11 extending from an aperture 12 at an outer side surface of the housing of the apparatus to a hemolyzing and measuring block 13 and further to a liquid detector and liquid conduit divider block 14, in which a liquid detector 28 is arranged. Below the lower side surface of the hemolyzing and measuring block 13, a light emitting device 35 constituted by a photo lamp is arranged. The intensity of the light emitted from the light emitting device 35 is detected by a light detector 101 constituted by a photodiode. The light detector is connected to a control circuit which supplies power to the light emitting device 35 and serves the purpose of maintaining a constant intensity of light radiated from the light emitting device 35. Part of the light emitted from the light emitting device or photo lamp 35 is transmitted through the blood sample contained in a cuvette 67 which constitutes part of the conduit extending through the hemolyzing and measuring block 13 and is optically processed in a monochromator assembly 36. Measuring signals generated in the monochromator assembly 36 are input to a signal processor 37 which further communicates with a central microcomputer 38 in which the measuring signals generated in the monochromator assembly 36 and processed in the signal processor 37 are further processed.

The Lundsgaard '769 patent further discloses that the optical system of the monochromator assembly 36 comprises an input part 47 for transmitting light from the light emitting device or photo lamp 35 to the blood sample contained in the cuvette 67 of the hemolyzing and measuring block 13, and an output part 48 for guiding or transmitting light transmitted through the blood sample contained in the cuvette 67 of the block 13 to a plurality of light detectors. The output part 48 comprises a biconvex lens 53, an optical screening device 54 having an aperture aligned in relation to the light transmission path of the biconvex lens, the block 13 and the input part 47, and further a concave mirror 57 and an optical grating device 58. From the aperture 55 of the optical screening device 54 the light is transmitted to the

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concave mirror 57 and further to the optical grating device 58 for separating the light transmitted to the grating device into monochromatic components. The light transmitted from the concave mirror 57 to the optical grating device 58, where part of the light transmitted to the optical grating device 58 is re-transmitted to the concave mirror 57 to the screening device 54. The screening device 54 is a plane and hollow device in which a plurality of light detectors or photodiodes 62 is housed. The individual light detectors or photodiodes 62 are exposed to monochromatic or substantially monochromatic light separated in the grating device 58 and reflected from the concave mirror 57 through slits or apertures 63 of the front surface of the screening device 54 facing the concave mirror 57. The light detectors or photodiodes 62 are constituted by photodiodes sensitive to light of a wavelength of approximately 400 nm-1000 nm and generate photodiode currents of the order of 1-400 nA. The logarithmic amplifier converts the photodiode current to 4 V/dec; 0 V=1 μ A. The outputs of the logarithmic amplifier 92 is converted to a normalized measuring signal representing the light intensities detected by the photodiodes 62 are input to an analog/digital converter 97. The output of the analog/digital converter 97 is connected to an interface input/output block 98 the output of which is connected to a bus 88.

The Ohta '617 patent discloses an arithmetic control mechanism of an optical CT apparatus for providing a tomographic image that calculates first light densities in output portions of an object on the basis of a numerical analysis method, when it is assumed that the object is divided into fine segments and all segments have the same value as an absorption coefficient under predetermined conditions equivalent to an actual measurement; and calculates second light densities in the output portions, when it is assumed that sequentially selected one of the segments has a specific value as an absorption coefficient under the predetermined conditions. Further, the mechanism calculates, as influences of the segments, ratios of the first to the second light densities, thereby obtaining an influence matrix corresponding to an arrangement of the segments; calculates relative ratios of the third light densities in the output portions on the basis of the actual measurements to the first light densities, thereby obtaining a relative ratio matrix corresponding to arrangements of input and output portions of the object; and performs a matrix calculation by using the influence matrix and the

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relative ratio matrix, thereby obtaining feature data of the segments for reconstructing a tomographic image of the object.

In contrast, embodiments of the present invention, as now claimed, are directed to methods, systems, and computer-readable medium encoded with a computer program capable of determining an amount of at least one molecular specie comprising a sample, with each molecular specie being indicated by a dye, from an image of the sample captured as image data by a color image acquisition device, such as a color camera or an RGB camera, in a video-microscopy system. An optical density of the sample is first determined from the image data, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel. A relative absorption coefficient for the dye indicating each molecular specie is then determined, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix. The optical density matrix is then multiplied by an inverse of the relative absorption coefficient matrix so as to form a resultant matrix for the pixel. The resultant matrix thus comprising the amount of each molecular specie, as indicated by the respective dye, for the pixel.

I. Response to the "Response to Arguments" in the Office Action

The Office Action presents various allegations to which the Applicants feel it is necessary and is compelled to respond and rebut.

A. The Office Action alleges that the Applicants argue for "a system involving a color image acquisition device, a plurality of dyes for staining the sample and the analysis of both sample and dye data in the red, green and blue channels of the color image acquisition device." The Applicants traverse this characterization for the following reasons. MPEP §2141.02(I) particularly notes that "[I]n determining the differences between the prior art and the claims, the question under 35 U.S.C. §103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.

Stratoflex, Inc. v. Aeroquip Corp., 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenck v.*

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Nortron Corp., 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983).” In the alleged characterization of the Applicants’ arguments, the Applicants submit that the Office Action is evaluating a “gist” or “thrust” of present invention, instead of particularly considering the combination of elements, as a whole, of the claimed methods, systems, and computer-readable mediums encoded with computer programs now pending in the present invention. In this regard, MPEP §2141.02(II) notes that “[d]istilling an invention down to the “gist” or “thrust” of an invention disregards the requirement of analyzing the subject matter “as a whole.” *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).”

B. The Office Action further alleges that the Applicants arguments target the references individually to show nonobviousness. More particularly, the Office Action alleges that the Applicants arguments regarding against the secondary references are directed to limitations found in the primary reference (the Applicants’ disclosure). The Applicants traverse this allegation for the following reasons. MPEP §2141.02(VI) recites that “[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Further, MPEP §§2142 and 2143 note that, “[t]o establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant’s disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991) (emphasis added). MPEP §2143.01(III) notes that “[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990).”

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In this regard, the Applicants assert that examination of the secondary references, each as a whole, is a necessary aspect of addressing an obviousness rejection. The Applicants also note that, to the extent that the Lambert-Beer law is applied as part of the claimed methods, systems, and computer-readable mediums encoded with computer programs now pending in the present invention, such an application is particularly claimed as being applied to pixels of an image of a sample obtained via the red, green and blue channels of a color image acquisition device (the optical density matrix for the pixel), in conjunction with characteristics of the dye(s), obtained independently of the sample via the red, green, and blue channels of the color image acquisition device, with such dye(s) used to treat the sample (the relative absorption coefficient matrix of the dyes).

In contrast, the background of the present application notes that a particular molecule may undergo a reaction with a particular dye to experience a change in color, that it is sometimes desirable to be able to determine an amount of a particular molecule in a sample, and that a color CCD digital camera can be used in combination with a microscopy system to capture images of a sample in the Red, Green and Blue channels (RGB) of the color CCD camera. As such, the background of the present application ("the primary reference" in the Office Action) does not teach or suggest applying the Lambert-Beer law in the manner recited in the claimed methods, systems, and computer-readable mediums encoded with computer programs now pending in the present invention. If such teaching or suggestion is not present in the primary reference, then such deficiency must be found in the secondary references in order to sustain an obviousness rejection. The Applicants evaluation of the secondary references is then necessarily directed to demonstrating that the secondary references do not teach or suggest determining an optical density matrix of a pixel of an image of a sample obtained via the red, green and blue channels of a color image acquisition device, and relating the same to a relative absorption coefficient matrix of the dye(s), obtained independently of the sample via the red, green, and blue channels of the color image acquisition device, with such dye(s) used to treat the sample, to determine the amount of each molecular specie, as indicated by the respective dye, for the pixel. In support of this conclusion, the Office Action particularly admits that the Ohia reference "is simply being used to show that use of relative absorption

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coefficient matrices in Lambert-Beer Law calculations is well known" and that the Lundsgaard reference "is being used to show that the Lambert-Beer Law is well known and can be applied to microscopy." That is, the admission in the Office Action supports the Applicants assertion that the primary reference, as well as the Ohta and Lundsgaard references, do not teach or suggest determining an optical density matrix of a pixel of an image of a sample obtained via the red, green and blue channels of a color image acquisition device, or determining a relative absorption coefficient matrix of the dye(s), obtained independently of the sample via the red, green, and blue channels of the color image acquisition device, with such dye(s) used to treat the sample

The Applicants therefore present arguments with respect to the secondary references in order to demonstrate that the secondary references do not teach or suggest applying the Lambert-Beer law in the particular manner recited by the Applicants (i.e., as applied to a pixel in an image of a sample in each of the red, green, and blue channels of a color image acquisition device) in the claimed methods, systems, and computer-readable mediums encoded with computer programs now pending in the present invention. Therefore, if the primary reference does not teach or suggest such a particular application of the Lambert-Beer law, and if the secondary references also do not teach or suggest such a particular application of the Lambert-Beer law, then the combination of the references cannot be sustained in arriving at the obviousness rejection asserted in the Office Action.

C. The Office Action further asserts that "the secondary references are being used to simply highlight information that is well known in the art and that a person of ordinary skill would find obvious to apply to the primary reference." The Applicants also traverse this allegation for the following reasons. MPEP §2143.01(IV) notes that "[a] statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to

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combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993)."

As previously noted, the primary reference, as well as the secondary references, do not teach or suggest methods, systems, and computer-readable mediums encoded with computer programs for determining an optical density of the sample from the image data corresponding to an image of the sample captured by a color image acquisition device in a video-microscopy system, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel, or for determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix, wherein the optical density matrix is then multiplied by an inverse of the relative absorption coefficient matrix so as to form a resultant matrix for the pixel, with the resultant matrix thus comprising the amount of each molecular specie, as indicated by the respective dye, for the pixel. In contravention to the assertions in the Office Action, the primary reference, as well as the Lundsgaard and Ohta references, do not teach or suggest applying a Lambert-Beer analysis to a pixel of an image of a sample obtained via the red, green and blue channels of a color image acquisition device (the optical density matrix for the pixel), in conjunction with characteristics of the dye(s), obtained independently of the sample via the red, green, and blue channels of the color image acquisition device, with such dye(s) used to treat the sample (the relative absorption coefficient matrix of the dyes). A theoretical Lambert-Beer analysis also does not teach or suggest applying the same to a pixel of an image of a sample obtained via the red, green and blue channels of a color image acquisition device (the optical density matrix for the pixel), in conjunction with characteristics of the dye(s), obtained independently of the sample via the red, green, and blue channels of the color image acquisition device, with such dye(s) used to treat the sample (the relative absorption coefficient matrix of the dyes).

In this regard, the Applicants assert that the allegations in the Office Action that "[a]spects relating to calculating the optical density are disclosed in Lundsgaard" and that "[a]spects relating to the relative absorption coefficient matrix are disclosed in Ohta" do not

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demonstrate the application of the Lambert-Beer analysis as particularly claimed in the methods, systems, and computer-readable mediums encoded with computer programs of the present invention. A purely mechanical combination of the primary reference (RGB image obtained by a color image acquisition device) with the Lundsgaard and Ohta reference (Lambert-Beer law) thus ignores the particularly recited limitations in the pending claims, as well as the direction of MPEP §2143.01(IV), which notes that an assertion that the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references.

II. Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 Are Patentable

In light of the rebuttal presented in Section I above, the Applicants have again reviewed the rejections and submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 are patentable over the cited references for a variety of reasons, any one of which is sufficient to remove the rejections against the claims. It is Applicants' opinion that:

A. The primary reference and the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, do not teach or suggest a system involving a color image acquisition device, a plurality of dyes for staining the sample, and the analysis of both sample and dye data for a pixel in an image of the sample in the red, green, and blue channels of the color image acquisition device; and

B. A person of ordinary skill in the art would not have an objective reason for combining the teachings of primary reference with the Lundsgaard '769 and Ohta '617 patents to arrive at the present invention as now claimed.

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Each of these reasons is discussed more fully below.

i. **The Cited References Do Not Teach, Suggest or Provide Motivation for the Combination as Alleged in the Office Action**

The Applicants first note that the Federal Circuit has consistently stated that a finding of obviousness requires a specific teaching, motivation, or suggestion to combine the teachings of individual items of prior art. See, e.g., *In Re Sang Su Lee*, No. 00-1158 (Fed. Cir. January 18, 2002) (factual question of motivation to combine is material to patentability and could not be resolved on subjective belief and unknown authority); *C.R. Bard, Inc. v. M3 Systems, Inc.*, 157 F.3d 1340, 1352 (Fed. Cir. 1998) (a showing of a suggestion, teaching, or motivation to combine is an essential evidentiary component of an obviousness holding); *In re Fritch*, 972 F.2d 1260, 1265 (Fed. Cir. 1992) (Examiner can satisfy burden of obviousness in light of combination only by showing some objective teaching leading to the combination); and *In re Fine*, 837 F.2d 1071, 1075 (Fed. Cir. 1988) (evidence of teaching or suggestion essential to avoid hindsight).

In this regard, the Applicants also note that MPEP §2141 explicitly states that, when “applying 35 U.S.C. 103, the following tenets of patent law must be adhered to:

- (A) The claimed invention must be considered as a whole;
- (B) The references must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination;
- (C) The references must be viewed without the benefit of impermissible hindsight vision afforded by the claimed invention; and
- (D) Reasonable expectation of success is the standard with which obviousness is determined.”

Furthermore, in determining the differences between the prior art and the claims, “the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious.” MPEP §2141.02, “Basic Considerations Which Apply to Obviousness Rejections,” citing *Stratoflex, Inc. v. Aeroquip Corp.*, 713 F.2d 1530, 218 USPQ 871 (Fed. Cir. 1983); *Schenk v. Nortron Corp.*, 713 F.2d 782, 218 USPQ 698 (Fed. Cir. 1983). (Emphasis added). The teaching or

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suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. MPEP §2143 citing *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Also, "[t]he requirement 'at the time the invention was made' is to avoid impermissible hindsight." MPEP §2141.01(III). In addition, "[a] prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984).

In light of these directives provided in the MPEP, the Applicants submit that separating background disclosure from each independent claim and then applying the cited references to the remainder, in the manner set forth in the Office Action, clearly **does not consider each independent claim as a whole** (i.e., the totality of the combination of elements, as recited). Furthermore, such rejections are **entirely contrary** to the requirement that **the teaching or suggestion to make the claimed combination and reasonable expectation of success must both be found in the prior art, and not in applicant's disclosure.** As such, the Applicants note that the background of the present application discloses that a particular molecule may undergo a reaction with a particular dye to experience a change in color, that it is sometimes desirable to be able to determine an amount of a particular molecule in a sample, and that a color CCD digital camera can be used in combination with a microscopy system to capture images of a sample in the Red, Green and Blue channels (RGB) of the color CCD camera. In making this assertion, **the Applicants inasmuch note that the Office Action clearly admits that the primary reference does not disclose any of the elements of the pending claims directed to analysis of the sample and dye image data.** That is, the Office Action (Page 6) clearly admits that the primary reference "does not expressly disclose determining an optical density of the sample from the image data so as to form a corresponding optical density matrix for the pixel; and multiplying the optical density matrix by an inverse of a relative absorption coefficient matrix so as to form a resultant matrix for the pixel, the relative absorption coefficient matrix comprising a relative absorption coefficient for each dye, independently of the sample, in each of the red, green, and blue channels, the resultant matrix comprising the amount of each molecular specie, as indicated by the respective dye, for the pixel." In this regard, the Applicants note that

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Claims 1, 14, 26, 41, 55, 64, and 77 have been amended to affirmatively recite that a relative absorption coefficient for the dye indicating each molecular specie is determined, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix.

Since the Office Action admits that the primary reference does not disclose any of the elements of the pending claims directed to analysis of the sample and dye image data, then such deficiency (i.e., all such elements of the pending claims such as, for instance, all elements of Claim 1) must be found in the secondary reference to support the asserted obviousness rejection. However, the Lundsgaard '760 patent is particularly directed to spectrophotometrically determining the concentration of a number of hemoglobin derivatives in whole blood, whereby light transmitted through the sample is detected by a plurality of light detectors or photodiodes. That is, the Lundsgaard reference directly analyzes the transmitted light intensity measured by the light detectors or photodiodes. Further, the hemoglobin derivative samples that are the subject of the Lundsgaard '769 patent are not treated with any dye. That is, the Lundsgaard '769 patent does not disclose the use of any dye.

The Office Action asserts that "Lundsgaard discloses determining an optical density of the sample from the image data." In this regard, the Lundsgaard reference measures transmitted light intensity and does not teach or suggest forming an image of the sample. Accordingly, the Lundsgaard does not teach or suggest determining an optical density of the sample from image data thereof, corresponding to an image of the sample captured by a color image acquisition device, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel. That is, the Lundsgaard reference does not teach or suggest applying a concept of determining an optical density to a pixel of an image captured by a color image acquisition device. The Applicants further note that since the Office Action clearly admits that this element is not taught or suggested by the primary reference, this deficiency must be found in the secondary reference(s) and, as such, by addressing the secondary reference(s), the Applicants are not "attacking references individually" as alleged in the Office Action. In addition, though the Applicants direct these arguments to the particular elements of Claim 1, now pending, the

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Applicants note that similar elements are also included in pending Claims 14, 26, 41, 55, 64, and 77 and any such arguments will also apply thereto even if not particularly addressed.

The Office Action further asserts that Lundsgaard discloses that the absorption coefficient is obtained independently of the sample in each of the channels, where "predetermined" absorption coefficients are considered to have been determined independently and image data at individual wavelengths is considered "equivalent to a channel." In this regard, the Applicants note that the corresponding element in the pending claims particularly requires that a relative absorption coefficient for each dye be determined, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix. That is, a relative absorption coefficient for each dye is determined, separately from the sample, in each of the red, green, and blue channels of the color image acquisition device, to form the relative absorption coefficient matrix. Furthermore, the Lundsgaard reference discloses that predetermined coefficients representing the light absorption characteristics of each of the hemoglobin derivatives comprising the blood sample at each of the individual wavelengths. As such, the Lundsgaard reference does not teach or suggest determining a relative absorption coefficient for a dye, independently of the sample, since the hemoglobin derivatives actually form part of the blood sample and the predetermined coefficients do not correspond to any dyes for treating the blood sample. With respect to the assertion in the Office Action that an individual wavelength as disclosed by Lundsgaard is considered "equivalent to a channel," MPEP §2144.06 particularly notes that "[i]n order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. *In re Ruff*, 256 F.2d 590, 118 USPQ 340 (CCPA 1958)." The Applicants submit that individual wavelengths used by the device disclosed by the Lundsgaard reference is not a functional or mechanical equivalent to the distinct red, green, and blue channels of a color image acquisition device, as recited in the claims of the present invention, and that such asserted equivalency is not recognized by the prior art (i.e., the Lundsgaard patent). Accordingly, the Applicants submit that the Lundsgaard reference does not teach or suggest determining a relative absorption coefficient for each dye,

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separately from the sample, in each of the red, green, and blue channels of the color image acquisition device, to form the relative absorption coefficient matrix, as particularly claimed in the present invention. The Applicants further note that since the Office Action clearly admits that this element is not taught or suggested by the primary reference, this deficiency must be found in the secondary reference(s) and, as such, by addressing the secondary reference(s), the Applicants are not "attacking references individually" as alleged in the Office Action.

Accordingly, the Applicants submit that the Lundsgaard '769 patent does not disclose determining an optical density of the sample from image data thereof, corresponding to an image of the sample captured by a color image acquisition device, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel. Further, the Applicants submit that the Lundsgaard '769 patent does not disclose determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix. Both such elements are recited in each of independent Claims 1, 14, 26, 41, 55, 64, and 77, now pending. As is evident from the pending claims, such elements include particular limitations that are not taught or suggested by either the primary reference (as particularly admitted in the Office Action) or the Lundsgaard reference, and do not amount to a mere use of the Lambert-Beer law, as alleged in the Office Action. That is, the Lundsgaard reference does not teach or suggest applying the Lambert-Beer law to image data from the red, green, and blue channels of a color image acquisition device. Further, characterization of the claimed invention is this manner in the Office Action, and alleging obviousness on the basis that both the primary reference and the Lundsgaard reference "deal with finding concentrations of biological components in a sample," ignores particular limitations associated with the elements of the pending claims as discussed extensively herein, thus failing to consider the claimed invention as a whole, as required by MPEP §2141.02. The alleged motivation of "improv[ing] identification of optical density of the sample and/or dye" is nowhere mentioned in either the primary reference or the Lundsgaard reference, and the Applicants respectfully request clarification of the meaning of such a statement.

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The Office Action further asserts that the primary reference and the Lundsgaard reference do not "expressly disclose the use of a relative absorption coefficient in Lambert-Beer law calculations." In this regard, the Applicants note that Claims 1, 14, 26, 41, 55, 64, and 77, now pending, more particularly recite determining a relative absorption coefficient for each dye, separately from the sample, in each of the red, green, and blue channels of the color image acquisition device, to form the relative absorption coefficient matrix. Notwithstanding these particular limitations which more accurately represent the pending claims, the Office Action admits that a relative absorption coefficient matrix comprising a relative absorption coefficient for each dye, separately from the sample, in each of the red, green, and blue channels of the color image acquisition device, is not disclosed by either the primary reference or the Lundsgaard reference. The Applicants further note that since the Office Action clearly admits that this element is not taught or suggested by the primary reference or the Lundsgaard reference, this deficiency must be found in the Ohta reference and, as such, by addressing the Ohta reference below, the Applicants are not "attacking references individually" as alleged in the Office Action.

The Ohta '617 patent cited in the Office Action is particularly directed to an optical computer tomographic apparatus for projecting light onto an object to be examined and reconstructing a tomographic image on the basis of the measurement value of the light transmitted through the object (as directly measured by a photodetector), and an image reconstruction method using optical computer tomography (CT) whereby a tomographic image is reconstructed in pseudocolor from the light intensities measured by the photodetector. The Ohta '617 patent further discloses that the "object" under consideration is a three-dimensional volume comprised of a plurality of volume elements (or "VOXELS"), whereby the image reconstruction method seeks to reconstruct a "slice" by considering the change in light transmissivity properties through a plurality of successive voxels. In addition, the Ohta '617 patent implements absorption coefficient values that are assumed under predetermined conditions for a measured CT volume element. That is, relative absorption coefficient values are assumed for segments of the sample itself. Accordingly, the Applicants submit that the Ohta reference does not teach or suggest determining a relative absorption coefficient matrix

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comprising a relative absorption coefficient for each dye, separately from the sample, in each of the red, green, and blue channels of the color image acquisition device, as particularly recited in the pending claims.

The Applicants further submit that the Ohta '617 patent is particularly directed to reconstructing a tomographic image in pseudocolor from the light intensities measured by the photodetector. That is, the Ohta reference directly analyzes the transmitted light intensity measured by the photodetector to reconstruct an image. Further, the CT volume element that is the subject of the Ohta '716 patent is not treated with any dye. That is, the Ohta '716 patent does not disclose the use of any dye. Therefore, the Ohta '617 patent does not disclose determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix, as particularly recited in the claims of the present invention, since neither a dye nor a color image acquisition device having red, green, and blue channels is used. Instead, the Ohta '617 patent discloses that any absorption coefficient values are assumed under predetermined conditions for a measured CT volume element of the sample itself.

Accordingly, as is evident from the pending claims, an element directed to determining a relative absorption coefficient matrix comprising a relative absorption coefficient for each dye, separately from the sample, in each of the red, green, and blue channels of the color image acquisition device includes particular limitations that are not taught or suggested by the primary reference, the Lundsgaard reference (as particularly admitted for both references in the Office Action), or the Ohta reference, and such an element is not merely involved Lambert-Beer law calculations, as alleged in the Office Action. That is, the Ohta reference does not teach or suggest determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels of a color image acquisition device, so as to form a corresponding relative absorption coefficient matrix for use in a Lambert-Beer law calculation. Further, characterization of the claimed invention is this manner in the Office Action, and alleging obviousness on the basis that both the primary reference, the Lundsgaard reference, and the Ohta

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reference "involve Lambert-Beer law calculations," ignores the particular limitations associated with the elements of the pending claims as discussed extensively herein, thus failing to consider the claimed invention as a whole, as required by MPEP §2141.02. The alleged motivation of "providing a basis for more accurate comparison of data from different color channels" is nowhere mentioned in the primary reference, the Lundsgaard reference, or the Ohta reference, and the Applicants respectfully request clarification of the meaning of such a statement.

The Applicants thus submit that the primary reference as well as the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, determining an optical density of the sample from image data thereof, corresponding to an image of the sample captured by a color image acquisition device, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel. Further, the primary reference and the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix. Thus, in view of these differences between embodiments of the present invention, as now particularly claimed in Claims 1, 14, 26, 41, 55, 64, and 77, and the primary reference and the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, the Applicants submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 are patentable over the primary reference and the Lundsgaard '769 and Ohta '617 patents cited in the Office Action.

ii. **A Person of Ordinary Skill in the Art Would Not Have an Objective Reason for Combining the Teachings of the Cited References as Alleged in the Office Action**

With respect to the person of ordinary skill in the art standard applied by the Office Action, it is particularly noted that "[t]here are three possible sources for a motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the

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knowledge of persons of ordinary skill in the art." MPEP §2143.01, "The Prior Art Must Suggest the Desirability of the Claimed Invention," citing *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998). In this regard, "[t]he level of skill in the art cannot be relied upon to provide the suggestion to combine references." MPEP §2143.01, "The Prior Art Must Suggest the Desirability of the Claimed Invention," citing *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999). Furthermore, "[a] statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references." MPEP §2143.01, "Fact That the Claimed Invention is Within the Capabilities of One of Ordinary Skill in the Art is Not Sufficient by Itself to Establish *Prima Facie* Obviousness," citing *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993); *In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1318 (Fed. Cir. 2000); and *Al-Site Corp. v. VSI Int'l Inc.*, 174 F.3d 1308, 50 USPQ2d 1161 (Fed. Cir. 1999).

With respect to the rejections of Claims 1, 14, 26, 41, 55, 64, and 77, the Office Action alleges that "[i]t would have been obvious for one skilled in the art, at the time the invention was made, to use Lambert-Beer's law as disclosed in Lundsgaard when processing the image data from each of the color channels in the applicant's admitted prior art as they both deal in finding concentrations of biological components in a specimen. This would result in improved identification of optical density of the sample and/or dye, thus providing motivation." The Office Action also alleges that "[i]t would have been obvious for one skilled in the art, at the time the invention was made, to use a relative absorption coefficient matrix as in Ohta when calculating the amount of a molecular specie as in [the primary reference] and Lundsgaard, as they both involve Lambert-Beer law calculations. Doing so would provide a basis for more accurate comparison of data from different color channels." The Applicants traverse these allegations, and thus traverse these rejections.

First, the application of the person of ordinary skill in the art standard in the Office Action to the obviousness rejection of Claims 1, 14, 26, 41, 55, 64, and 77 based upon the

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combination of the Lundsgaard '769 and Ohta '617 patents, as well as "the applicant's admitted prior art," is in direct contravention to MPEP §2143.01, which explicitly states that "[t]he level of skill in the art cannot be relied upon to provide the suggestion to combine references."

Further, as previously discussed, the primary reference and the Lundsgaard '769 and Ohta '617 patents, either separately or in combination, clearly do not teach or suggest, whatsoever, determining an optical density of the sample from image data thereof, corresponding to an image of the sample captured by a color image acquisition device, in each of a red, green, and blue channel of the color image acquisition device and for a pixel in the image, so as to form a corresponding optical density matrix for the pixel, or determining a relative absorption coefficient for the dye indicating each molecular specie, independently of the sample and in each of the red, green, and blue channels, so as to form a corresponding relative absorption coefficient matrix.

In addition, the meanings of the motivations to combine alleged in the Office Action are not particularly clear to the Applicants (i.e., it is not clear what the motivational statements mean in technical terms) and the alleged motivations are nowhere mentioned by any of the primary reference, the Lundsgaard reference, or the Ohta reference. Thus, the alleged motivations to combine do not provide any objective reason as to why one having a system involving a color image acquisition device, a plurality of dyes for staining the sample, and the task of analyzing sample and dye data in the red, green, and blue channels of the color image acquisition device, would be motivated to use the Lambert-Beer law as disclosed in Lundsgaard and Ohta to analyze a pixel in an image captured by the color image acquisition device, when neither the primary reference, the Lundsgaard reference, nor the Ohta reference teach or suggest such an application. As such, the alleged motivation to combine primary reference with the Lundsgaard '769 and Ohta '617 patents is also in direct contravention to MPEP §2143.01, which explicitly states that the "[a] statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a prima

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facie case of obviousness without some objective reason to combine the teachings of the references."

Thus, in view of these factors, the Applicants further submit that Claims 1, 11, 14, 26-28, 36-38, 41, 42, 50-52, 55, 64-66, 72-74, 77, 78, and 86-88 **are patentable** over the primary reference and the Lundsgaard '769 and Ohta '617 patents cited in the Office Action.

III. Claims 2-10, 12, 13, 15-25, 29-35, 39, 40, 43-49, 53, 54, 56-63, 67-71, 75, 76, 79-85, 89, and 90

Claims 12, 13, 24, 25, 39, 40, 46, 53, 54, 68, 75, 76, 89, and 90 were also rejected in the Office Action as being obvious over the primary reference and the Lundsgaard '769 and Ohta '617 patents in view of U.S. Patent No. 5,734,498 to Krasieva *et al.* Claims 2-10, 15-23, 29-35, 43-49, 56-63, 67-71, and 79-85 were further rejected in the Office Action as being obvious over the primary reference and the Lundsgaard '769 and Ohta '617 patents in view of U.S. Patent No. 6,819,787 to Stone *et al.*

As previously discussed, Claim 1, upon which Claims 3-10, 12, and 13 depend; Claim 14, upon which Claims 16-25 depend; Claim 26, upon which Claims 29-35, 39, and 40 depend; Claim 41, upon which Claims 43-49, 53, and 54 depend; Claim 55, upon which Claims 57-63 depend; Claim 64, upon which Claims 67-71, 75, and 76 depend; and Claim 77, upon which Claims 79-85, 89, and 90 depend, **are patentable** over the primary reference and the Lundsgaard '769 and Ohta '617 patents. Thus, in response, the Applicant further submits that the present invention, as claimed in Claims 3-10, 12, 13, 16-25, 29-35, 39, 40, 43-49, 53, 54, 57-63, 67-71, 75, 76, 79-85, 89, and 90, is patentable over the primary reference and the Lundsgaard '769, Ohta '617, Krasieva '498, and Stone '787 patents. As such, the Applicant respectfully requests withdrawal of these rejections.

Conclusion

In summary, the primary reference and the Lundsgaard '769, Ohta '617, Krasieva '498, and Stone '787 patents, either separately or in combination, **do not** teach, suggest, or provide motivation for embodiments of the present invention, as now claimed in Claims 1, 14, 26, 41, 55,

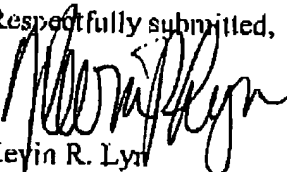
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64, and 77. Accordingly, in view of these differences between the Applicant's invention and primary reference as well as the Lundsgaard '769, Ohta '617, Krasieva '498, and Stone '787 patents, it is submitted that the present invention, as defined by the pending claims, is patentable over the prior art cited in the Office Action. As such, Claims 1, 3-14, 16-55, and 57-90 are believed to be in condition for immediate allowance.

In conclusion, for the reasons set forth above, the Applicant submits that all claims now pending are in condition for immediate allowance. Accordingly, notice to such effect is respectfully requested at the Examiner's earliest opportunity.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

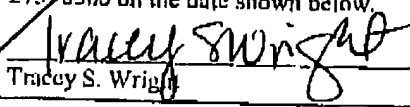
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